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REMARKS

Applicant's attorney wishes to thank the Examiner for the careful consideration given this case. Claims 1, 3, 7, 9, 11, 13, 15, 17, 19, 27, and 32 are pending in this case. Claims 2, 4-6, 8, 10, 12, 14, 16, 18, 20-26, and 28-31 are cancelled. Claim 32 identical to originally-filed Claim 5. No new matter is introduced by Claim 32. Claims 1, 9, and 11 are amended. No new matter has been introduced through these amendments.

This response addresses those issues raised in the Office Action dated August 21, 2003. It is believed that the present amendments and following remarks render all pending claims allowable. Reconsideration of the claims as amended is respectfully requested.

Before remarks are presented on the merits of the pending Office Action, the appropriateness of the finality of the pending Office Action will be discussed. The Examiner issued the present Office Action as a Final Office Action. The Examiner cites to the Applicants' previous amendment of Claim 5 as the basis for the finality of the present Office Action. As discussed during the telephonic interview of November 21, 2003, the Applicants' representative committed a clear clerical error in the submission of the previous response that has lead to the present situation. As noted correctly by the Examiner, the second half of Claim 5 was inadvertently deleted. No amendment to Claim 5 was intended as is clearly indicated by the "(original)" status indicator found following the numbered portion of the claim. The confusion that this clerical error generated led to the issuance of the present Final Office Action. Applicants sincerely apologize for this error. Further, the Applicants respectfully request the retraction of the finality of the present Office Action for this reason alone.

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In addition, the Examiner goes on to introduce new art (Haugland et al.) as the basis of a new rejection in the pending Office Action. MPEP § 706.07(a) provides explicit instruction to when the issuance of a Final Office Action is appropriate:

Under present practice, second or any subsequent actions on the merits shall be final, except where the examiner introduces a new ground of rejection that is neither necessitated by the applicant's amendment of the claims nor based on information submitted in an information disclosure statement filed during the period set forth in 37 CFR 1.97(c) with the fee set forth in 37 CFR 1.17(p).

It is respectfully submitted that the present obviousness rejection based, in part, on Haugland et al. is a new ground of rejection that was neither necessitated by the Applicants' amendment of the claims nor based on information submitted in an Information Disclosure Statement filed since the issuance of the last Office Action. Accordingly, withdrawal of the finality of the present Office Action is respectfully requested.

Applicants have cancelled Claims 2, 4-6, 8, 10, 12, 14, 16, 18, 20-26, and 28-30 in response to the Examiner's comments regarding the earlier restriction requirement, without prejudice.

The Examiner notes that the Applicants must provide a corrected substitute computer-readable copy of the "Sequence Listing" and a statement that the content of the paper and computer readable copies are the same and include no new matter. Applicants are timely submitting the computer-readable format, a hard copy of the sequence listing, and the required statement concurrently via mail to the Biotechnology Systems Branch. Copies of the sequence listing and the required statement are being submitted herewith for the convenience of the Examiner.

The Examiner rejects Claim 5 under 35 U.S.C. § 112, ¶2 as being indefinite for failing to particularly point out and distinctly claim the subject

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matter of the invention. As noted above, the confusion of the Examiner is well placed and caused by th Applicants' representative's inadvertent deletion of the second half of Claim 5. Applicants have reintroduced the original content of Claim 5 as Claim 32 to avoid all confusion. Reconsideration and withdrawal of this rejection is sincerely and respectfully requested.

The Examiner rejects Claims 1, 3, 5, 7, 9, 11, 13, 15, 17, and 27 under 35 U.S.C. § 103(a) as being unpatentable over Brush et al. (U.S. Patent No. 5,986,086; the '086 patent) in view of Haugland et al. (U.S. Patent No. 5,719,031; the '031 patent).

Herein, Claim 1 is amended to include a the limitation where the substituent C represents a monovalent group derived from a fluorescent dye having no sulfonic acid group and no phosphoric acid in a molecule, and sulfonamide group or a lower alcohol group. This amendment is supported by the description on lines 11-13 of page 10, as well as Compounds 5-8 on page 21 of the specification. It is respectfully submitted that the claims in their present form are in condition for allowance. Notification to that effect is earnestly solicited.

Brush et al. disclose non-sulfonated cyanine dyes for labeling nucleotides, but do not teach a dye having a sulfonamide group or a lower alcohol group. Haugland et al. teach using sulfonamide in the dye to attach to a nucleotide (Col. 7, line 35). It should be noted that in Haugland et al., the sulfonamide is used as the linkage which is a spacer or linker for attaching the functional group on the polymer and the reactive group of the fluorophore. In contrast, in the present invention, the sulfonamide is not used as a linkage but rather as a water soluble group which gives an advantageous effect in connection with the solubility of the dye and the fluorescent intensity, as mentioned hereinbelow.

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It should be noted that the sulfonamide group in Haugland et al. does not achieve the advantageous effects of the present invention, since it is used as the linkage which is a spacer or linker for attaching the functional group on the polymer and the reactive group on the fluorophore, rather than being used as a group which is free at its terminal as in the present invention (see compounds 5 to 8 on page 21 of the present application). Since Haugland et al. do not teach the property of a sulfonamide as a water-soluble group, there is no motivation to combine Brush et al. with Haugland et al. Such combination is the result of impermissible hindsight on the part of the Examiner. Further, even if Brush et al. is combined with Haugland et al., the feature of the present invention is not generated from such a combination, since Haugland et al. teaches the use of sulfonamide group only as the linkage but not as a group on a free terminal that delivers water solubility to the molecule.

The advantage of the use of a dye having a sulfonamide group or lower alcohol group is described in the second paragraph of Page 10 of the specification of the present application in the following manner:

However, especially fluorescent dyes of high molecular weights sometimes become to be insoluble due to reduction of functional groups having these negative charges. In one aspect of the present invention, the problem for these insolubility is solved by introducing a water-soluble functional group into a chromophore of a dye. For example, in one embodiment of the present invention, the fluorescent nucleotide is characterized in that it has a water-soluble group other than a sulfonic acid group in its fluorescent dye component. Water-soluble functional groups which can be introduced into the fluorescent dye include sulfonamide, polyether, lower alcohol, sugar chain, tertiary amine, quaternary ammonium salt and the like.

The advantageous effect of the present invention is demonstrated in the Examples of the present application. The fluorescent intensities of Compounds 5-8 are stronger than the comparative dye Cy-5-dUTP (from Amersham) or Cy-3-dUTP (from Amersham), as shown in Tables 1 and 2 on pages 27 and 28 of the present application. Please note that Cy5 and Cy3 are

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dyes having a sulfonic acid (salt), but not having a sulfonamide group or a lower alcohol group, as presently claimed. The advantage of the present invention is achieved by using a a dye having no sulfonic acid group and no phosphoric acid and having a sulfonamide or a lower alcohol. The advantageous effect of the presently-claimed invention is not taught or fairly suggested by either Brush et al. or Haugland et al., either singly or in combination. Reconsideration and withdrawal of the present obviousness rejection is respectfully requested.

The Examiner rejects Claim 19 under 35 U.S.C. § 103(a) as being unpatentable over Brush et al. (of record) in view of Haugland et al. (of record), in further view of Mao et al. Applicants respectfully submit that the present obviousness rejection is inappropriate for the reasons cited above regarding Brush et al. and Haugland et al. Mao et al. does not cure the deficiencies of the cited prior art. Reconsideration and withdrawal of this obviousness rejection is respectfully requested.

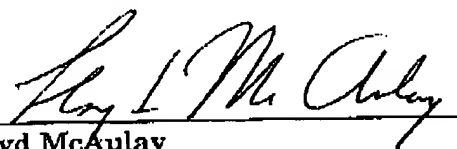
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In view of the amendments to the claims and the remarks presented her in, it is respectfully submitted that the present application is in condition for final allowance and notice to such effect is requested. If the Examiner believes that additional issues need to be resolved before this application can be passed to issue, the undersigned invites the Examiner to contact him at the telephone number provided below.

Respectfully submitted,

Dated: November 21, 2003

By


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